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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,294	04/02/2001	Chil-Yong Kang	9611-16	4835

1059 7590 12/16/2004

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EXAMINER	
PARKIN, JEFFREY S	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/762,294	KANG ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,7 and 31-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 6, 7, and 31-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Amendment

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the amendment filed 29 September, 2004. Claims 1, 6, 7, and 31-40 are currently under examination.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37-40 are are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed toward vaccine compositions for the prevention and treatment of HIV infection through the administration of a recombinant HIV-1 virus wherein the natural signal sequence has been replaced by a heterologous signal sequence.

The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation

necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The disclosure fails to provide adequate guidance pertaining to the correlates of protective immunity that are required for a protective or therapeutic immune response. In order to practice the claimed invention, the skilled artisan would require a knowledge of the correlates of protective immunity in order to assess if the vaccine composition of interest is producing the desired immune response. However, the disclosure is silent concerning this aspect of vaccine development and it is not readily manifest what type of immune response (i.e., humoral, cell-mediated, or both) is required for protection and therapeutic immune responses.

2) The disclosure fails to provide adequate guidance pertaining to the quasispecies nature of HIV-1 infection. The vast genotypic and phenotypic diversity of HIV-1 means that any putative vaccine must be capable of neutralizing a number of different isolates, strains, and clades in order to be effective. However, the specification fails to provide any guidance pertaining to this subject.

3) The disclosure fails to provide any data from an art-recognized animal model demonstrating that the claimed vaccine compositions are truly effective immunogens. Before administering the claimed compositions, the skilled artisan would require a demonstration that said compositions were capable of inducing the desired immune response in the intended host.

4) The prior art teaches that HIV-1 vaccine development is extremely unpredictable (Haynes et al., 1996; Haynes, 1996; Burton

and Moore, 1998; Letvin, 1998; Lee, 1997). To date there are no FDA-approved vaccines for the prevention or treatment of HIV-1 infection. This is due to several factors including the lack of understanding of the correlates of protective immunity, the lack of adequate animal models in which to assess vaccine efficacy, and the quasispecies nature of HIV-1 infection.

Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Li *et al.* (1994). Li and colleagues disclose the preparation of recombinant HIV-1 viruses wherein the wildtype gp160 signal sequence has been replaced with the MSS or IL-3SS (see ABSTRACT, p. 256). Thus, contrary to applicants' arguments, this teaching meets all of the claimed limitations.

Claim 1 is rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Li *et al.* (1996). Li and colleagues disclose the preparation of recombinant HIV-1 viruses wherein the wildtype gp160 signal sequence has been replaced with the mellitin signal sequence or interleukin-3 signal sequence (see ABSTRACT, p. 9606). Thus, this teaching meets all of the claimed limitations.

35 U.S.C. § 103(a)

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 6, 7, and 31-36 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Li *et al.* (1994) in view of Daniel *et al.* (1992). Li and colleagues disclose the preparation of recombinant HIV-1 viruses wherein the wildtype gp160 signal sequence has been replaced with the MSS or IL-3SS (see ABSTRACT, p. 256). This publication also discloses the preparation of recombinant HIV-1 viruses wherein the positive charge of the HIV-1 signal sequence has been reduced to contain no more than zero or one positively

charged amino acids (see pp. 271-272). The preparation of *nef*-deficient avirulent viruses is not disclosed. Daniel *et al.* (1992) teach that *nef*-deficient SIV produces a virus that is replication-impaired and apthogenic. Furthermore, vaccine compositions comprising this virus protected macaques against viral infection. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to prepare recombinant HIV-1 viruses with modified signal sequences, as taught by Li *et al.* (1994), and to further include a *nef*-deletion in the construct, as provided by Daniel *et al.* (1992), since this would provide a recombinant virus that is replication-impaired and expressed to high quantities. The skilled artisan would be motivated to prepare such a construct because of obvious safety considerations (i.e., the virus would obviously be safer to handle in manufacturing viral antigens for diagnostic assays). Applicants' arguments have been carefully considered but are not deemed to be persuasive for the reasons set forth *supra*.

Claims 6, 7, and 31-36 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Li *et al.* (1996) in view of Daniel *et al.* (1992). Li and colleagues disclose the preparation of recombinant HIV-1 viruses wherein the wildtype gp160 signal sequence has been replaced with the MSS or IL-3SS (see ABSTRACT, p. 9606). The preparation of *nef*-deficient avirulent viruses is not disclosed. Daniel *et al.* (1992) teach that *nef*-deficient SIV produces a virus that is replication-impaired and apathogenic. Furthermore, vaccine compositions comprising this virus protected macaques against viral infection. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to prepare recombinant HIV-1 viruses with modified signal sequences, as taught by Li *et al.* (1996), and to further include a *nef*-deletion in the construct, as provided by Daniel *et al.* (1992), since this would provide a recombinant virus that is replication-

impaired and expressed to high quantities. The skilled artisan would be motivated to prepare such a construct because of obvious safety considerations (i.e., the virus would obviously be safer to handle in manufacturing viral antigens for diagnostic assays). Applicants' arguments have been carefully considered but are not deemed to be persuasive for the reasons set forth *supra*.

Finality of Office Action

Applicants' amendment necessitated any and all new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). **A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.**

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, James C. Housel, can be reached at (571) 272-0902. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Formal communications may be submitted through the official facsimile number which is (703) 872-9306. Hand-carried formal communications should be directed toward the customer window located in Crystal Plaza Two, 2011 South Clark Place, Arlington, VA. Applicants are directed toward the O.G. Notice for further guidance. 1280 O.G. 681. Informal communications

may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

12 December, 2004